PREVALENCE AND PATTERNS OF CUTANEOUS LESIONS IN DIABETES MELLITUS

DISSERTATION SUBMITTED FOR M.D. DEGREE

EXAMINATION OF

BRANCH I GENERAL MEDICINE

MARCH 2010

TIRUNELVELI MEDICAL COLLEGE

THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU.

CERTIFICATE

This is to certify that this dissertation entitled **'Prevalence and Pattern of cutaneous lesions in Diabetes Mellitus** submitted by **Dr.G.Panneer Selvam** to the faculty of Medicine, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD Degree Branch I (General Medicine), is a bonafide research work carried out by him under our direct supervision and guidance.

Dr.J.Kaniraj Peter M.D.,

Professor & HOD
Department of Medicine,
Tirunelveli Medical College,
Tirunelveli.

Dr.A.Kanagaraj M.D.,

Unit Chief,
Department of Medicine,
Tirunelveli Medical College,
Tirunelveli.

ACKNOWLEDGEMENT

It gives us great pleasure to acknowledge all those who guided, encouraged and supported me in all the successful completion of my dissertation.

I whole heartedly thank **THE DEAN**, Tirunelveli Medical College for having permitted me to carry out, this study at Tirunelveli Medical College.

First and foremost I wish to thank **Prof. Dr.J.Kaniraj Peter M.D.**, Prof & HOD, Dept. of Medicine for having guided me throughout the period of this work.

My sincere thanks to **Prof. Dr.A.Kanagaraj M.D.**, my Unit Chief, who gave me this topic, and guidance throughout the work.

I owe my heartiest thanks to Prof. **Dr.P.Nirmala Devi M.D.,** (Dermatology) for valuable suggestion, support and expert guidance throughout the work.

I sincerely thank my Assistant Professor **Dr.M.Paulraj B.Sc., M.D.,** and my medical registrar **Dr.Rajagopala Marthandam M.D.,** for the kind words of advice, constructive criticism and co-operation which enabled me to complete this study.

I thank all Professors, Assistant professors, technical staffs.

I thank all the patients who gave full cooperation and support throughout my study.

CONTENTS

1. INTRODUCTION

Diabetes mellitus (DM) is a worldwide problem and the most common endocrine disorder. Its prevalence is increasing in the present scenario of a sedentary lifestyle in the general population. Abnormalities of insulin and elevated blood glucose level lead to metabolic, vascular, neurological and immunological abnormalities. Affected organs include the cardiovascular, renal and nervous systems, eyes and the skin. [1] The skin is affected by both the acute metabolic derangements and the chronic degenerative complications of diabetes. Although the mechanism for many diabetes associated skin conditions remains unknown, the pathogenesis of others is linked to abnormal carbohydrate metabolism, other altered metabolic pathways, atherosclerosis, microangiopathy, neuron degeneration and impaired host mechanisms. [2] The association of certain skin diseases with DM has been fairly well recognized with an incidence rate ranging from 11.4 [3] to 71%. [4]

2. AIM OF THE STUDY

Aims & objectives:

1. To assess the prevalence of diabetes mellitus association with skin disorder in population in and around Tirunelveli in all population attending the out patient and inpatient in Tirunelveli medical college hospital

2. To assess the correlation of skin diseases with systemic manifestation of diabetes mellitus.

3. To assess the pattern of skin lesions which are commonly associated with diabetes.

3. REVIEW OF LITRATURE

DIABETES

Definition

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both.

Criteria for diagnosis

Fasting $\geq$ 126mg%

Postprandial $\geq$ 200mg%

Symptoms of diabetes plus Random Blood Glucose$\geq$200mg%

Classification[5]

Type 1 Diabetes mellitus

Type 2 Diabetes mellitus

Other Specific Types

Gestational Diabetes

Type 1 Diabetes Mellitus

Definition

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycemia.

Caused by a complex interaction of genetics, environmental factors, and lifestyle choices

Classified on the basis of a pathogenic process leading to hyperglycemia

Results from pancreatic beta-cell destruction, usually leading to absolute insulin deficiency

Type 1A DM results from autoimmune beta-cell destruction, which leads to insulin deficiency.

Type 1B DM lacks immunologic markers indicative of an autoimmune destructive process of beta cells, but like type IA DM, it is a ketosis-prone insulin deficiency that develops by unknown mechanisms.

Epidemiology

Worldwide prevalence: dramatic increase over past 2 decades and projected to increase further

Incidence

Incidence varies by geography.

Believed to reflect the frequency of high-risk human leukocyte antigen (HLA) alleles among ethnic groups in different geographic locations

Scandinavia: highest incidence (e.g., Finland, 35 cases per 100,000 persons yearly)

Northern Europe and U.S.: intermediate rate (8–17 cases per 100,000 persons yearly)

Pacific Rim: much lower rate (Japan and China, 1–3 cases per 100,000 persons yearly)

Age of onset

Can develop at any age, but often in childhood or early teens

Usually <30 years of age

Of persons who develop DM after 30 years of age, ~5–10% have type 1A DM.

Type 2 DM

A heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production

Preceded by a period of abnormal glucose homeostasis, classified as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)

Common characteristics

Development of DM after 30 years of age

Obese (80%)

Elderly persons may be lean.

May not require insulin initially

May have associated conditions (e.g., hypertension, cardiovascular disease, dyslipidemia, or polycystic ovary syndrome)

Insulin resistance often associated with central obesity and hypertriglyceridemia

Epidemiology

DM Worldwide prevalence: greatly increased over past 2 decades

Prevalence

By age (in 2000)

<20 years: 190 cases per 100,000 persons

≥20 years: 8,600 cases per 100,000 persons

>65 years: 20,100 cases per 100,000 persons

By sex

Most age ranges: equal in men and women

>60 years of age: slightly more men than women

By race (in the U.S. in 2000)

African Americans: 13,000 cases per 100,000 persons

Hispanic Americans: 10,200 cases per 100,000 persons

Native Americans (American Indians and Alaska natives): 15,500 cases per 100,000 persons

Non-Hispanic white persons: 7,800 cases per 100,000 persons Type 2 DM

Incidence/prevalence varies by geography (likely owing to genetic, behavioral, and environmental factors).

Highest: certain Pacific islands

Intermediate: India and U.S.

Relatively low: Russia and China

Prevalence is expected to increase more rapidly than type 1 DM because of increasing obesity and reduced activity levels

Age of onset

Can develop at any age

Typically develops with increasing age, >30 years of age

Age of diagnosis is decreasing in some ethnic groups.

Occurs at an earlier average age in ethnic groups other than non Hispanic whites

Marked increase among overweight children and adolescents.

Other specific types of diabetes

Maturity-onset diabetes of the young (MODY) and genetic defects of beta-cell

Function. Characterized by mutations in:

Hepatocyte nuclear transcription factor (HNF) 4α (MODY 1)

Glucokinase (MODY 2)

HNF-1α (MODY 3)

Insulin promoter factor 1 (MODY 4)

HNF-1β (MODY 5)

NeuroD1 (MODY 6)

Mitochondrial DNA

Proinsulin or insulin conversion

Diagnostic Approach

National Diabetes Data Group and World Health Organization criteria for DM

Based on the following premises:

Fasting plasma glucose (FPG) and response to oral glucose load vary among normal persons.

DM is defined as the level of glycemia at which diabetes-specific complications occur rather than as deviations from the population-based mean.

Hemoglobin A1C

- Standard method for assessing long-term glycemic control

  6%: 7.5 mmol/L (135 mg/dL)

  7%: 9.5 mmol/L (170 mg/dL)

  8%: 11.5 mmol/L (205 mg/dL)

A 1% increase in the hemoglobin A1C level translates into a 2.0-mmol/L (35-mg/dL) increase in the mean glucose level.

Screening laboratory tests for DM-associated conditions

- Microalbuminuria

  Spot urine microalbumin/creatinine ratio (beginning 5 years after onset of type 1 DM)

Microalbuminuria is defined by a microalbumin/creatinine ratio >30 mg/g creatinine.

- Dyslipidemia

  Fasting lipid profile (annual)

- Thyroid dysfunction

  Serum thyroid-stimulating hormone

Factors to consider in developing goals of therapy

Age

Ability to understand and implement complex treatment regimen

Presence and severity of complications

Ability to recognize hypoglycemic symptoms

Presence of other medical conditions or treatments that might alter response to therapy

Lifestyle and occupation (e.g., possible consequences of experiencing hypoglycemia on the job)

Level of support available from family and friends

Life expectancy at time of diagnosis

Presence of microvascular complications

Hemoglobin A1C level: <7.0%

Provide patient with educational and pharmacologic resources necessary to reach goal.

Monitor/treat DM-related complications.

Comprehensive care

Best accomplished by a multidisciplinary team approach o Primary care provider and/or endocrinologist or diabetologist o Certified diabetes educator o Nutritionist

Subspecialists with experience in treating DM-related complications

- Neurologist
- Nephrologist
- Vascular surgeon
- Cardiologist
- Ophthalmologist
- Podiatrist
- Dermatologist

Goals of diabetes management during hospitalization

Avoid hypoglycemia.

Optimize glycemic control.

Maintain near-normal glucose levels with insulin.

Transition the patient back to outpatient diabetes treatment regimen.

Optimal glycemic control in hospitalized patient

Preprandial glucose level: <6.1 mmol/L (100 mg/dL)

Postprandial glucose level: <10 mmol/L (180 mg/dL)

Complications - Acute complications

Diabetic ketoacidosis.

Hyperglycemic hyperosmolar state

Primarily seen in patients with type 2 DM

Hyperosmolar Hyperglycemic State

Chronic complications

Responsible for majority of morbidity and mortality associated with DM

Leading cause of adult blindness, nontraumatic lower-extremity amputation, and end- stage renal disease in the U.S.

Risk increases with duration of hyperglycemia.

Usually becomes apparent in second decade of hyperglycemia

Microvascular

1. Eye disease

Retinopathy (nonproliferative or proliferative)

Macular edema

Other nonvascular eye disease (cataracts, glaucoma)

2. Neuropathy

Sensory and motor (mononeuropathy and polyneuropathy)

Autonomic

3. Nephropathy

Macrovascular

Cardiovascular Complications of Diabetes Mellitus for details.

Coronary artery disease

Peripheral vascular disease

Cerebrovascular disease

G I T

Gastroparesis

Diarrhea

Genitourinary

Lower extremity

Amputation

DM is the leading cause of nontraumatic lower-extremity amputation in the U.S.

Foot ulcers and infections

The interaction of several pathogenic factors promote development.

Neuropathy

Disordered proprioception

Abnormal foot biomechanics

Peripheral arterial disease

Poor wound healing

Approximately 15% of patients with DM develop a foot ulcer.

A significant subset undergo amputation; risk is 14–24% with that ulcer or subsequent ulcers.

Risk factors for foot ulcers or amputations

Male sex

DM >10 years

Peripheral neuropathy

Abnormal structure of foot (bony abnormalities, callus, thickened nails)

Peripheral arterial disease

Smoking

History of previous ulcer or amputation

Poor glycemic control

Infectious

Persons with diabetes have a greater frequency and severity of infection.

Osteomyelitis

Pneumonia

Urinary tract infections

Skin and soft-tissue infections

Several rare infections occur almost exclusively in DM.

Rhinocerebral mucormycosis Emphysematous infections of gall bladder and urinary tract

"Malignant" or invasive otitis externa

Fournier's syndrome, a necrotizing fasciitis most commonly confined to the groin

Dermatologic

Common features

Protracted wound healing

Skin ulcerations

Xerosis and pruritus

Diabetic dermopathy (pigmented pretibial papules or "diabetic skin spots")

Bullous diseases (shallow pretibial ulcerations or erosions)

Necrobiosis lipoidica diabeticorum

Rare disorder that predominantly affects young women with type 1 DM, neuropathy, and retinopathy.Begins in the pretibial region as an erythematous plaque or papules that gradually enlarge, darken, and develop irregular margins, with atrophic centers and central ulceration.May be painful

Granuloma annulare

Scleredema

Lipoatrophy and lipohypertrophy Can occur at insulin injection sites o Unusual with human insulin

Metabolic syndrome

(also referred to as Syndrome X or Insulin Resistance Syndrome)

Describes a cluster of CVD risk factors and metabolic alterations associated with excess body fat.

WHO Definition

IGT / IFG/T2DM + any of the two below

Increased Waist-Hip Ratio (M:>0.9, F: >0.85)

Elevated Blood Pressure>140/90 mm Hg

Elevated Triglycerides>150mg/dl

Low HDL cholesterol

Microalbuminuria

DERMATOLOGIC LESIONS IN DIABETES

Numerous skin lesions are associated with either type 1 or type 2 diabetes mellitus, specific chronic complications of the disease, use of antibiotic drugs, and certain endocrine and metabolic disorders that cause secondary diabetes mellitus. Varies cutaneous manifestations are significantly associated with diabetes compared to control groups[6]

Classification of Dermatologic lesions of diabetes mellitus[7]

There is no strict classification of skin lesions related to diabetes mellitus, therefore grouping them under the following headings will give us an idea about various types of skin lesions occurring in diabetes.

Dermatologic lesion associated with but not specific for diabetes mellitus (SKIN MARKERS)

- Prurites
- Necrobisis lipoidica diabeticorum
- Granuloma annulare
- Diabetic dermopathy
- Scleroderma like syndrome
- Acanthosis nigricans
- Diabetic bulla

Skin alterations due to diabetic complications

- Diabetic foot
- Cutaneous infections associated with diabetes
    - Furunculosis
    - Carbuncle
    - Pyoderma
    - Candiasis
    - Dermatophytosis
    - Erythrasma
    - Xanthomatosis
    - Pycomycosis
    - Malignant otitis media

1. **Dermatological changes associated with neurovascular complications**
    - Macroangiopthy
    - Microangiopathy
    - Diabetic neuropthy
2. **Dermatologic complications of diabetes treatment**
    - With oral hypoglycemic agent
    - With insulin

3. **Endocrine syndromes with skin alterations and diabetes mellitus**

   - Migratory necrolytic erythema in glucogonama

4. **Dermatoses that are more common in diabetes mellitus**

   - Perforating dermatosis
   - Vitiligo
   - Lichen planus
   - Eruptive xanthoma
   - Kaposi sarcoma
   - Bullous pempigoids
   - Dermatitis herpatiformis
   - Psoriasis

Various types of dermatological lesions in details

1. Dermatologic lesion associated with but not specific for diabetes mellitus

PRURITIS

Genralized pruritis was once considered a typical symptoms of diabetes but its frequency is unknown. Studies have failed to provide a statistical basis for this belief. [8] . A higher rate of pruritis is found in liver disease, uremia, parasitic infestations, endocrine disorders(thyroid),

malignant disease, hematological and metabolic diseases and as a side effects of some drugs.

Genralized pruritsis associated with diabetes complications of chronic renal insufficiency, occationally neuropathy(irritation of nerve ending can cause). High level of urea in the blood cause the skin to itch. Candidiasis or dermatophytosis may underlie pruritis in diabetic patient. Anorectal pruritis is often caused by candidiasis in diabetic .

Ringworm is appear on the feet. groin, trunk, scalp,or nails. Itching in the elderly diabetes is not a feature of hyperglycemia but rather a manifestation of xerosis. Simple lupricants and low potency corticosteroids application should prove helpful.

NECROBISIS LIPOIDICA DIABETICORUM

Occurring in 7 % of the diabetic patients[9]. These relatively asymptomatic more common in women. It is one of the cutaneous markers of diabetic. In insulin users the onset is considered to occur earlier than type 2 diabetes or non diabetes. The lesions are characteristically found on the anterior and lateral surfaces of lower legs i.e in the pretibial and medial malleolar region. They may also present on the face ,arms and trunks. There may be one or several lesions, either unilateral or bilateral. The lesions begins as a small dusky-red elevated nodule with a sharply circumscribed border. It slowly enlarged to turn into a plague of irregular

outline, flattened, and eventually depressed as the dermis become more atrophic.

The color turns more brownish-yellow except for the border, which may remain red. The epidermis is smooth or slightly scaly and atrophic. Delicate vessels can be seen through the surface. The lesions may be anesthetic or reduced sensation to pin prick and to fine touch due to destruction of cutaneous nerve.

The chronic lesion of NLD are indolent; shallow, often painful ulcer frequently appear as long standing lesion. In the early stages, NLD may resemble granuloma annulare or sarcoid, but a well developed plaque is characteristic and easily recognized. The primary pathologic changes are in the lower dermis, where collagen is markedly altered with focal area of loss of normal structure., swelling basophilia and distortion of bundles (necrobiasis). There is increased collaginase and aggregation of inflammatory cells in the lesion which later gives the appearance of foam cells account for the designation of '**lipoidica**'. The nature of association with diabetes and its pathogenesis remains unclear. Because NLD occurs both IDDM and NIDDM, its pathogenesis cannot be related to genetic factors, underlying autoimmune disease or other cause of diabetes. The treatment of NLD is not very satisfactory progression of lesion does not correlate with normalization of the hyperglycemia. Topical application of glucocorticoids under occlusion or by intralesional injection may afford

some improvement of active lesion. Ultraviolet treatment has been found to be control when it is flaring.

GRANULOMA ANNULARE

It is a benign necrobiotic condition associated with lesion similar to NLD, the only difference being the absence of atrophy. This is a skin disease usually seen in children and young adults. It is occasionally seen with diabetes. It is characterized by red spots in the initial stages that expand outwards in a ring like fashion. The hands especially the fingers, on dorsal or lateral aspect of the hands and elbows (forearm) are commonly affected. Patient with widespread graluma annulare need to be screened for diabetes mellitus. Mostly it is asymptomatic and resolve spontaneously.

DIABETIC DERMMOPATHY

It is common skin lesion occurring in diabetes . It is prominenent in males whom are more than 50 years of age[10] . It is seen even in euglucemic, endocrine disease and in healthy individuals. The presence of small vessela changes had led to term diabetic dermopathy. The lesions are asymptomatic, irregularly shaped patches occurring primarily over the anterior legs; their surface are depressed and they have a light brown color. The pigmentation is due to deposition of hemosiderin in histiocytes and extravascular superficial erythrocytes. These lesion can occur in

upper arms,thigh, and any bony prominence. Lesions appears crops and gradually resolve over 12 to 18 months. The disorder is asymptomatic requiring no treatment except for protecting the area from any trauma and secondary infection. Use of bioocclusive dressing is recommended.

SCLERODERMA-LIKE SYNDROME

Scleroderma-like syndrome, reduced joint mobility, waxy skin syndrome are synonymous denoting one and the same skin disorders. Reduced joint mobility probably is the earliest complication of diabetes and a characteristic finding in children and adolescents after only 10 years of diabetes duration. The metacorpophalangeal joint and proximal interphalengeal joint are usually first involved. Reduced extention ,initially active ,then also passive, is is observed. Flexion may for long remain completely preserved. Clinicl signs include impossible extension of the palm on the table and impossible clasping hands as in prayer. Restriction of passive extension of the interphalangeal and metacarpo-phalangeal is the most important from the diagnostic point of view. The skin become thickened, with waxy appearance,in about one third of patients[11] .Such skin lesions resemble sclerodermic skin. Historically, dermal collagen thickening and elastic fibres reduction are observed.

ACANTHOSIS NIGRICANS

Acanthosis nigricans appears as velvety hyperpigmented pappilomatous hyperplasia of epidermis primarily in flexural areas like axillary, inquinal, and inflammatory folds, and in creases of the neck. Acanthosis nigricans is associated with two forms. The severe form is usually found with advanced malignancy particularly gastro intestinal tract. The more limited form is more frequently found in association with a variety of endocrinopathies, including acromegaly, cushing syndrome,and polycystic ovary disease. A variety of endocrine diseases and acanthosis nigricans suggest that insulin resistance is a common denominator even in the absence of overt diabetes.

Acanthosis nigricans has been associated with all three form of insulin resistance

Type A in which insulin resistance is due to receptor defects resulting in decreased insulin binding.

Type B in which insulin resistance is conferred by effects of circulating antireceptor antibodies.

Type C in which post receptor defect including abnormalities in signal transduction such as autophosphorylation of the receptor and activation of tyrosine kinase inhibit insulin action[12]. The use of keratolytic agents such as salicylic acid can improve the appearance cosmetically,

DIABETIC BULLAE

The bullae appears spontaneously, commonly in the dorsum and sides of the lower legs sometimes on forearm and hands. It may range from millemeters to centimeters. The lesions are often bilateral and containing clear fluids. There is no surrounding erethema. Generally the bullae heel in several weeks without significant scarring and they may recur[13]. The bullae are subepidermal and ultrastructural studies have demonstrated the plane of separation to in the basement membrane zone above the basal lamina. Neither trauma or immune mechanism have been implicated. Usually do not need any treatment apart from prevention of secondary infection.

2. Skin alterations due to Diabetic complications

Neurovascular and ischaemic changes and foot ulceration(diabetic foot)

Diabetic foot is a serious complication which results from confluence of multifactorial pathogenic mechanisms. Neuropathy (motor, sensory & autonomic) and diabetic angiopathy are the contributing factors for its development, the neuropathy being the major factor. Laceration which may be complicated with necrosis, gangrene and osteomyelitis, accentuated plantar arches and hammer toes with inter digital maceration leading to bacterial and fungal infections and loss of ankle jerk and vibration sensation are the features of diabetic foot. Because of its serious

nature it requires special attention. Prevention is by far more relavant than cure. Hence care of the foot must become a routine in diabetic patients.

Cutaneous infections associated with diabetes

Poorly controlled or undiagnosed diabetics have a greater susceptibility to bacterial and fungal infections of skin. The most frequently encountered infections are staphylococcal pyodermas such as furunculosis and carbuncles, candidiasis erythrasma and dermatophytosis.

Furunculosis (boils)

The word boil refers to swelling. There is extended involvement of the hair follicle including the perifollicular region in the dermis and subcutaneous tissue, i.e, there is folliculitis as well as perifolliculitis. It is caused by staphylococcus aureus. Boils are common during adolescence and early adult season. Isolated furuncles appear and many lesions may develop together. Factors like diabetes mellitus, exfolliative dermatitis and intake of systemic steroids may be responsible for their increased frequency and greater severity. Those furuncles which do not discharge on the surface are called blind boils.

Carbuncle

A group of boils which show deep infections of contiguous follicles with S.aureus. The infection spreads from one follicle to the other usually

not via the surface but through the sub cutaneous tissue. The lesion starts as a painful, tender, firm to hard indurated lump with a course similar to but more protracted than that of a furuncle. It is associated with intense inflammatory changes in the surrounding and underlying tissues. Pus is discharged not necessarily due through the follicular openings but from any point. The common sites are back of the neck, shoulders, hips and thighs. It is frequently associated with diabetes mellitus. If the underlying conditions are controlled and appropriate therapy instituted, healing takes place leaving a scar; otherwise toxaemia and even death may follows.

Pyodermas

The advent of antibiotics and tighter control of diabetes has markedly reduced the incidence and morbidity of pyodermas which were formerly considered as serious complications. Lower extremities constitute a particular hazard of diabetic patient. The associated atherosclerosis and peripheral neuropathy lead to ulceration and gangrene as well as poor wound healing.

Candidiasis (moniliasis)

Candida albicans is a common complication in poorly controlled diabetics[14] . They show considerable improvement when diabetes is controlled. Candidal infections of the skin may resemble those caused by other dermatophytes but are most common where skin is moist and in

contact with itself, e.g., groin, perineum, breast, axillae and vulvovaginal areas. Nail infections start at the base, forming ridges, often accompanied by paronychia. It is the infection of the web space brtween 3rd and 4th finger. In the mouth white curd like patches are seen, which can be scraped away leaving a bleeding base. Atrophy of the gums and angular stomatitis are common in elderly.

Balanitis and Balanoposthitis

Balanitis is common among elderly and uncircumscribed patients. Balanoposthitis usually presents with itching, pain, erotions, cracks and whitish scales on the terminal portions of the prepuce. Diabetes is often the underlying disease. In diabetics or immunosuppressed, a severe edematous, ulcerative balanitis may occur. Phimosis has been observed as a common complaint in diabetic men and recurring candidal infection is usual cause.

Dermatophytosis

It is encouraged by sharing of wash places and ringworm is due to dermatophyte fungi infection. There are three main genera: Trichophyton; Microsporum; and Epidermophyton. Clinical features depends on the site and species.

Tinea pedis

Most common type of fungal infection. The sharing of wash places and swimming pools encourages it. Infrequent washing of socks and use of

occlusive footwear encourages relapses. It may present as Interdigital scaling, diffuse powdery scaling of soles and recurrent bouts of vesiculation of soles. The organisms involved are T.rubrum, T.mentagrophytes var.interdigitale, and E.floccosum.

Tinea unguium:

Toe nail infection is more common than finger nail infection and is often accompanied by tinea pedis. Usually only few nails or involved. Changes first occur at the free edge of the nail, which becomes yellow and crumbly. Thickening of nail and separation of the nail from the nail bed follows. T.rubrum is usual cause.

Tinea manuum

It is usually asymmetric and involves palms (dry powdery scaling picking out of creases) more often than back of hands.

Tinea cruris

It infects men more often than women and causes well demarcated redness and peripheral scaling of groins and upper thighs. A few vesicles or pustules are usually seen with the lesions. Eruption is often unilateral or asymmetric and itchy.

Tinea corporis:

It is archetypal ringworm eruption. Erythematous scaly plaques expand slowly and clear in the center, leaving a ring-like pattern are characteristic.

Erythrasma

The lesions are reddish, in fact, reddish brown in early stage which is not generally observed at this stage. After a period of time, the lesions become brownish-black with irregular but very well defined margins. They are smooth but later appear creased and even finely scaly. The sites of predilection are genito crural folds, axillae and submammary folds. The coryneforms causing erythrasma are seen in large sections of population in the interdigital web spaces where they produce only mild scaling. The lesions fluoresce coral red under wood's light or UVA light, due to coproporphyrin III production by bacteria. If the patient has recently taken bath, the fluorescence may not be observed, as the porphyrin is soluble in water.

Xanthomatosis

Eruptive xanthomas are characteristic but uncommon complication of diabetics associated with more sustained hyperlipidaemia affecting plasma triglycerides and cholesterol more than phospholipids and hyperglycemia with glycosuria. The decreased lipoprotein lipase activity in insulin dependent diabetics results in the accumulation of serum

triglycerides, whose levels are occasionally highly elevated to produce eruptive xanthomas.

Cutaneous xanthomas results from deposition of lipid in the histocytes in the dermis or sub cutaneous tissue. It may be pruritic initially. Rapid regression of these lesions occurs hyperlipidaemia is brought under control.

Xanthelasma

It occurs hyperlipidaemic states including diabetes. It does not regress with therapy for diabetes. A yellowish discoloration of the skin of the palms, soles and nasolabial folds due to deposition of carotene present in excess quantities in plasma may be associated with hyperlipidaemia even in the absence of xanthomatosis in diabetes.

Phycomycetes infection

Hyperglycemia may permit organisms that are pathogenic to produce infection in traumatized skin, which may lead to gangrene and loss of the limb. There are various factors , which help the phycomycetes establish and lead to the infection. These factors include pre-exsisting leg ulcers, nonhealing surgical wounds, deep seated fungal infections, etc., treatment must be aggressive, consisting of correcting acid-base balance, debridement of devitalized tissue and intravenous antifungal therapy. Patients with uncontrolled diabetes mellitus and ketosis may be

predisposed to deep fungal infections or rhinocerebral mucormycosis of the turbinates, septum, palate, maxillary and ethmoid sinuses[15] .

Malignant otitis media

It is caused Pseudomonas aeroginosa. It is an uncommon but a very serious infection. Initially there is purulent discharge and in the external ear canal. It occurs commonly in diabetic men. It begins as a cellulitis and progress to chondritis , osteomyelitis, and infective cerebritis. It usually has fatal outcome.

3. Dermatologic changes associated with neurovascular complications of diabetes

Macroangiopathy

Patients with diabetes mellitus have a slightly higher incidence and prevalence of large vessel disease compared with control subjects. In patients with IDDM or NIDDM, both low-density lipoprotein cholesterol and VLDL triglycerides are risk factors. Atherosclerosis of the arteries of the legs results in skin atrophy, hair loss, coldness of toes, nail dystrophy, pallor on elevation and mottling on dependence. A reliable sign of large vessel disease is dependent rubor with delayed return of color after pressure has been applied to skin[16] .

Microangiopathy

The role of diabetic microangiopathy is not completely understood. The signs include diabetic dermopathy, pigmented purpura, erysipelas

such as erythema, NLD,periungual telangiectases and diabetic foot[17] . Other signs of microangiopathy include cutaneous reactive hyperemia and reduced capillary flow on cold or warm challenges of the patients with IDDM and those with MIDDM, as measured by Laser Doppler flowmerty.

The thickening of the vessel walls, perivascular deposition of material reactive with periodic acid-schiff stain, and clumping of the elastic fibers in the papillary dermis are produced by a combination of intimal hyperplasia and increased deposition of type IV collagen within and around the vessel wall. The space between the pericytes and the endothelial cells is wider and the cytoplasmic processes that formed the contact point between them is longer and thinner than normal, suggesting a possible explanation for increased permeability[18] . The capillary leakage leads to the loss of albumin and water and the platelets have a higher tendency to aggregate. As a result, increased whole blood and plasma viscosity creates a sluggish microcirculation.

Diabetic rubiosis is a peculiar rosy reddening of the face, sometimes of the hands and feet, which may be observed in longstanding diabetics. It has been attributed to diabetic microangiopathy or decreased vascular tone.

Diabetic neuropathy

Elderly patients in whom the onset of diabetes is insidious are especially at risk of developing diabetic neuropathy. A common

neuropathy in diabetes mellitus is a distal, symmetric, mixed polyneuropathy involving both motor and the sensory nerves[19].

The skin manifestations of autonomic neuropathy in diabetes mellitus are disturbances in sweating and peripheral hyperaemia with eryrhema, edema, and atrophy. Motor neuropathy of the feet leads to imbalance between flexor and extensor muscles, displacement of fat pads and subluxation of digits.

Typical signs of sensory neuropathy in diabetes mellitus are paraesthesia with loss of temperature and pain sensation, as well as aching and burning of the legs that worse at night. The combination of motor and sensory neuropathy along with mechanical factors and micriangiopathy plays a major role in development of diabetic foot.

Immunohistochemical studies of nerves in diabetic skin have demonstrated depletion of neuropathies. The antidepressants such as desipramine and amitryptylline that inhibit the membrane pump mechanism for the reuptake of neuropeptides have proved effective in diabetic peripheral neuropathy.

4. Dermatologic complication due to treatment of diabetes

Oral Hypoglycemic Drugs

The cutaneous complications of oral hypoglycemic agents are few. The first generation sulphonylureas such as chlorpropomide and tolbutamide, and usually develop in the first two months of treatment. Allergic skin reactions are uncommon. They are usually mild and self limited. Patients may present with intermittent or persistent pruritus or a maculo popular rash. Other cutaneous reactions which occur occasionally include urticaria and erythema multiforme, which may progress to steven-johnson syndrome. Other rare skin manifestations include erythema nodosum and purpura as well as exacerbation of porphyria cutanea tarda and generalized hypersensitivity reactions.

The chlorpropomide alcohol flush occurs in the patients taking this drug. The reactions usually occur within 15 mins after ingestion of alcohol. It causes flushing, headache, tachycardia and dyspnoea that gradually subsides after an hour.

Insulin

Cutaneous complications due to insulin therapy used to be common before advent of newer insulins. Allergic reactions to insulin may be immediate or delayed. Serious generalized reactions such as urticaria and anaphylaxis are rare.the immediate local reaction becomes is probably IgE mediated. It starts as erythema, becomes urticarial in 30 mins and subsides

in an hour. The delayed reaction is more common. It is due to delayed hypersensitivity. About 2 weeks after the initiation of insulin therapy, a pruritic nodule develops within 1to2 days at the site of injection, lasts for days and heal with hyper pigmentation and scarring. Localized induration, ulceration and scar formation and development of ketosis may result from faulty injection techniques. Idiosyncratic reactions are very rare and include pigmentation and occasionally keloid formation. Skin reactions resembling acanthosis nigricans has been reported.

Insulin lipoatrophy and lipohypertrophy which are the complications of the insulin injections, are rare after the introduction of newer insulins. Lipoatrophy presens as circumscribed atrophic plagues showing atrophy of the subcutaneous fat at the site of the insulin injection, and rarely shows complete resolution. It may be due to a local immune response to insulin injection[20] .

Lipohypertrophy is a soft dermal nodule . The overlying skin appears normal at the site of injection. It may be due to the lipogenic action of the insulin.

Insulin edema occur on the abdomen and legs area are most common and usually a self-limiting complication which appear shortly after starting or increasing the dose of insulin. It is commonly seen in women and is unrelated to the cardiac or renal disease. The pathogenesis is unclear. Ephedrine is the drug of choice[21].

5. Endocrine syndromes with the skin alterations and diabetes mellitus

Glucagonoma

It is the most characteristic endocrine syndrome manifesting with skin alteration and the diabetes mellitus and is often diagnosed later. The dermatosis is the clical clue. It is due to tumors of alpha cells glucogon secreting portion of the pancreas. It has four componenets

- Hypersecretion of glucagons
- Diabetes that is usually mild
- Weight loss
- Necrolytic migratory erethema.

Histologically they resemble pustular psoarisis, with the feature of intracellular edema in the upper extremities.,acanthosis and subcorneal pustulosis. Necrolytic migratory erethema resolves after extirpation of the tumor, which in the majority of the cases is the treatment of choice[22].

6. Dermatosis reported to be more common in diabetics than in non diabetics.

Kaposi sarcoma

It is a multiple idiopathic hemorrhagic sarcoma, which manifest primarily as multiple nascular nodules in the skin and other organs. It predominently affects males. The lesions begins in the legs as multiple purple macules, nodules or plagues. Later the other area of the skin,

mucous membranes and the internal organ may be involved. Histological pictures reveal accumulation of the spindle cells forming vascular slits containing erethrocytes[23] . Diabetes mellitus has been reported with greater than expected frequency in the classic Kaposi sarcoma.

Perforating dermatosis

There are several acquired cutaneous disorders having a common histological denominator the transepidermal elimination of the degenerative materials, chiefly collagen and elastic fibres. Many are seen in patient with chronic renal failure, particularly those on dialysis and with IDDM, or NIDDM. The size of the papules ranges from 2 to 10 mm in diameter, often with a keratotic plugs. The most patients are middle aged often block, and more often in men than women. Improvement of the itchy lesions is not achieved easily but retinoic acid[24] . and ultraviolet therapy has been useful.

Vitiligo

It is disease with a diminished or absent function of the melanocytes resulting in macular depigmentation and is found in mostly in perioral regions and also on the extensor aspect of the extremities. It is asymptomatic. Vitiligo occurs with a greater incidence than expected in patient with maturity onset diabetes. It is also reported in association with IDDM and other autoimmune disorders of the adrenal and thyroid gastric parietal cells.

Lichen planus

An increased incidence of the diabetes mellitus and abnormal insulin response to glucose challenge have been claimed in patients with lichen planus. [25] . There are two types of lichen planus one is immunogenic type and another is a metabolic defect type, both being associated with diabetes mellitus.

Yellow nails

The lesions commonly involve distal hallux and is quite common in diabetics[26] .The earliest sign is yellow or brown color of the distal part of the hallux nail plate. Later a cannry-yellowish discoloration occurs on the nails. It can involve finger nails and other toe nails during the later stage of the disease.

Eruptive xanthomas

It is frequently occur in uncotroller diabetes. The eruptions are multiple, firm, yellowish in color, waxy papules ranging from 1 to 4 mm in diameter, appearing in crops. They are mostly located on the extensor surfaces. The firm nontender papules are present on the knees,elbow,back.buttocks and trunk.the lesions are itchy, sometimes tender, surrounded by erethematous halo.they shows koebner's phenomena[27] . The underlying factor in hyperlpidemic status is decreased lipoprotein lipase activity or increased LDL, making chylomicrons less able to compete LDL for lipoprotein lipase. There are some evidence that

eruptive xanthomas in diabetics result from macrophage incorporating plasma lipoprotein forming foam and xanthoma cells. With correction of hyperlipidemia and hyperglycemia, the lesions involute, sometimes with post inflammatory hyperpigmentation and occationally scars.

Bullous pemphigoids

Theoretically, their association may be due to the lower threshold of the diabetes in traumatically induced blisters or on the basis of enzymatic glycosylation. Steroids sometimes even immunosuppressive drugs may be appropriate.

Dermatitis herpatiformis

The HLA association of the diabetes and the dermatitis herpetiformis may be a possible explanation for the these two appearing together more frequently than expected.

Psoriasis

It is a multifactorial disease of unknown origin. There are a distinct pattern of associated diseases existing with psoarisis. Systemic disorders such as hypertension and diabetes are often seen in these patients. The resion for the diseases to occur in psoarisis patients have been related to nutritional factors of hypercaloric dietary habits[28] .

4 .MATERIALS AND METHODS

Study design:

Cross sectional study.

Methods of selection:

1. All patients attending out patient department in Tirunelveli medical college hospital in medicine OPD, Dermatology OPD, and inpatients in Tirunelveli medical college hospital with or without referrence from various govt/private hospital in and around tirunelvel zone in tamil nadu.
2. cross sectional study

Inclusion Criteria:

1. All adults.
2. Individuals who attending all OPDs including Diabetic OPD during the period of May - October 2008 and May - October 2009 till reaching the quota of 50 diabetic patients in a month.
3. Patients admitted as IP in any of the Departments during the above period with diabetes.

Exclusion criteria:

1. Age less than 12 yrs.

Materials:

1. basis on the clinical examination

2. basis on the blood sugar value for the diagnosis of the diabetes

Six hundred diabetic patients attending the diabetic clinic, medical out-patient department and skin out-patient department and different wards of patients in Tirunelveli Medical College Hospital, Tirunelveli, were studied. A detailed history and clinical examination, especially for the presence of cutaneous lesions, was carried out during the period from May 2008 to October2009. After investigations, patients with abnormal blood glucose levels were taken for study. Fundus and routine blood, stool and urine examinations were carried out in all the patients. Blood sugar estimation was done by alkaline copper reduction method. Scrapping and direct KOH examination and culture for fungus in sabouraud's agar and gram staining and culture of the pus was done to identify the type of bacterial organism in selected cases. Histopathological examination of the skin sections was carried out wherever necessary to confirm the diagnosis.

5. RESULTS

Table 5.1.1 OPD DM PATIENTS DETAILS MONTHWISE IN 2008

2008	OPD	SL	DM	M	F	TYPE I	TYPE II	UNCLASSIFIED	SL IN DM
MAY	422	32	50	24	26	3	40	7	11
JUNE	350	42	50	29	21	4	42	4	12
JULY	322	33	50	23	27	2	38	10	8
AUG	480	37	50	26	24	2	41	7	9
SEPT	384	41	50	28	22	4	40	6	11
OCT	504	37	50	26	24	3	38	9	10
TOTAL	2462	222 9.1%	300 12.2%	156 52.0%	144 48.0%	18 6.0%	239 79.7%	43 14.3%	61 20.3%

Table 5.1.2 OPD DM PATIENTS DETAILS MONTHWISE IN 2009

2009	OPD	SL	DM	M	F	TYPE I	TYPE II	UNCLASSIFIED	SL IN DM
MAY	340	32	50	23	27	3	41	6	9
JUNE	401	27	50	28	22	2	43	5	8
JULY	378	25	50	24	26	3	43	4	8
AUG	420	30	50	22	28	2	40	8	9
SEPT	390	35	50	27	23	3	39	8	9
OCT	512	37	50	25	25	3	38	9	8
TOTAL	2441	186 7.6%	300 12.3%	149 49.6%	151 51.4%	16 5.3%	244 81.3%	40 13.3%	51 17%

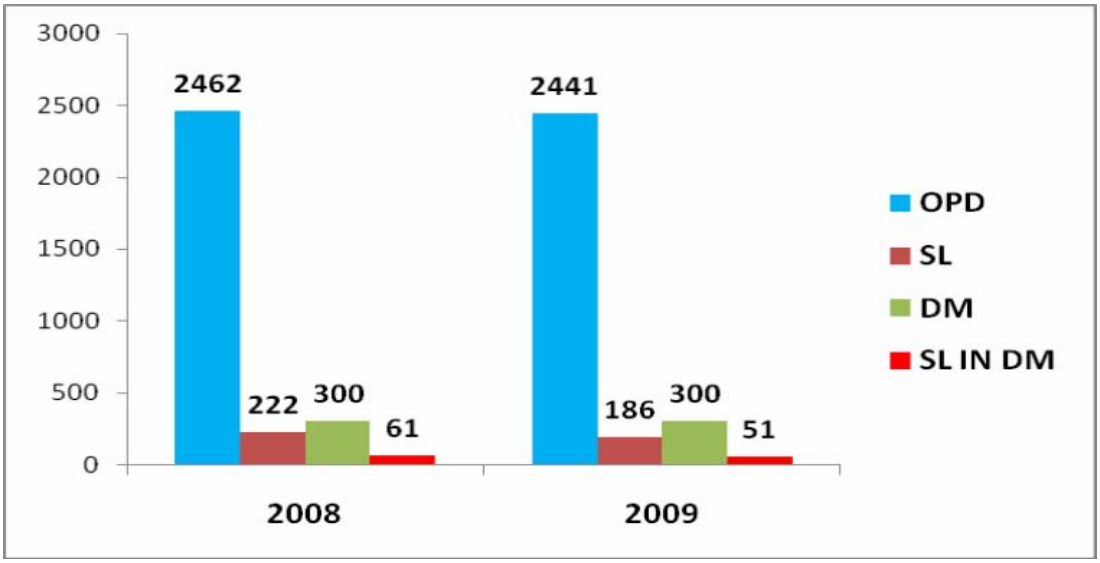

Fig.5.1. OPD patients analysis year wise.

Table 5.2.1 IP DM PATIENTS DETAILS

YEAR	TOTAL DM	MALE	FEMALE	TOTAL SKIN LESIONS	MALE	FEMALE
2008	422	220	202	70	36	34
2009	307	156	151	64	33	31
TOTAL	729	376 51.6%	353 48.4%	134 18.4%	69 51.5%	65 48.5

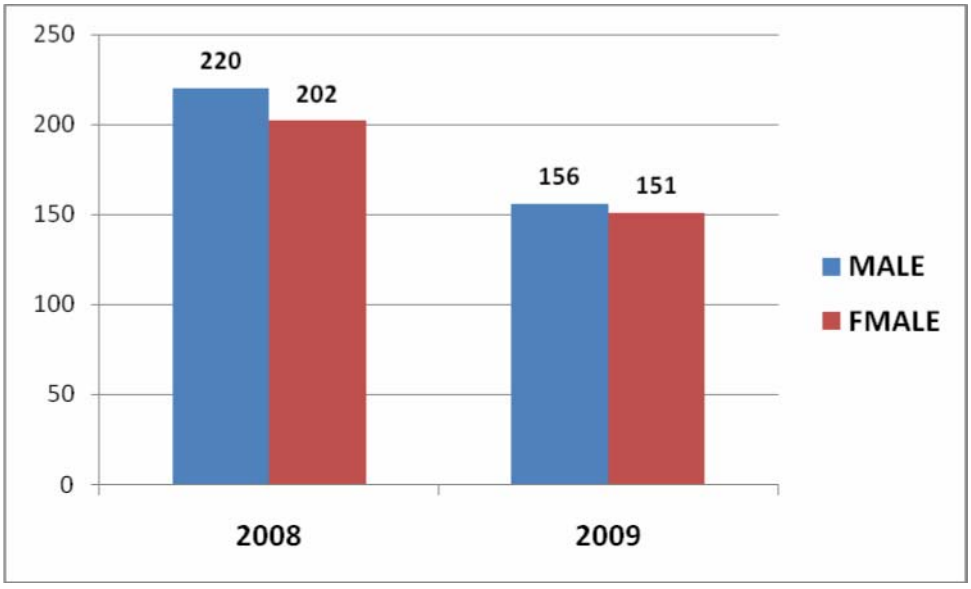

Fig.5.2 .1 Sex distributions among IP DM patients

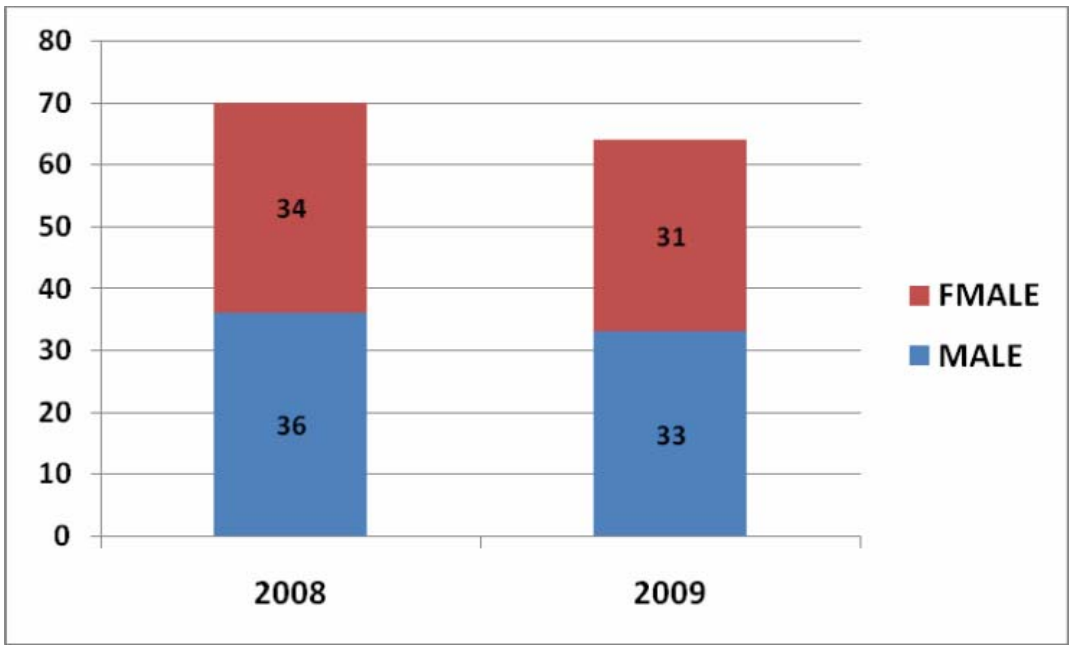

Fig-5.2.2 Sex distribution in DM IP patients with skin lesions.

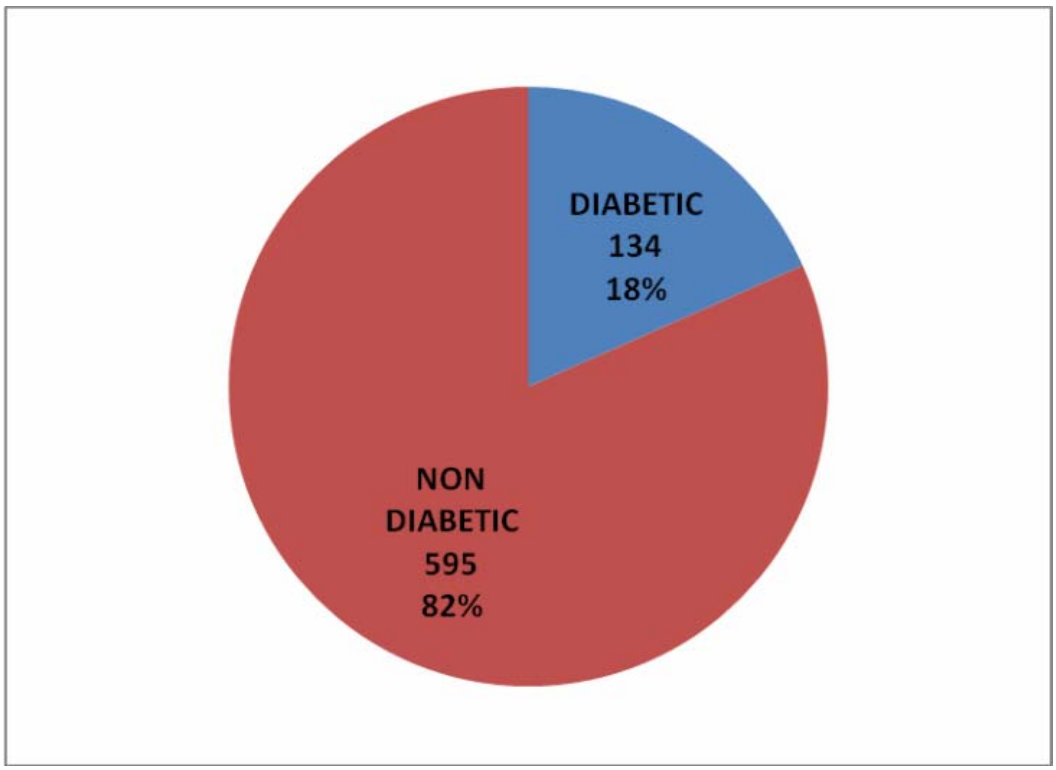

Fig. 5.2.3. Proportion of Skin lesions among IP DM patients.

Table 5.3 COMBINED OPD AND IP DM PATIENTS WITH SKIN LESIONS IN DETAILS

	DM	MALE	FEMALE	SKIN LESIONS	MALE	FEMALE
OPD	600	305	295	112	57	55
IP	729	376	353	134	69	65
TOTAL	1329	681 51.2%	648 48.8%	246 18.5%	126 51.2%	120 48.8%

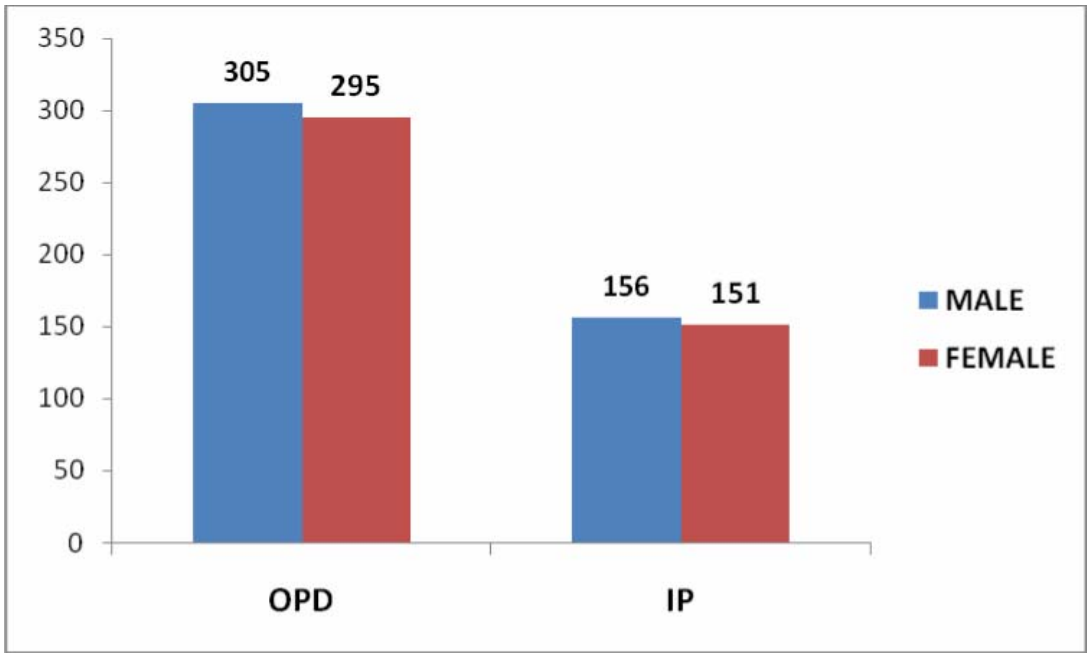

Fig. 5.3.1 Sex Distribution in Diabetes

Fig. 5.3.2 Sex distribution in Skin Lesions associated with diabetes

ANALYSIS OF DIABETIC PATIENTS (N=112) WITH SKIN LESIONS

Table 5.4 SEX DISTRIBUTION

SEX	FREQUENCY	PERCENTAGE
MALE	55	49.1
FEMALE	57	50.9
TOTAL	112	100

Table 5.5 AGE DISTRIBUTION

SR.NO	AGE GROUP	FREQUENCY	PERCENTAGE
1	≤30	14	12.5
2	31 - 40	15	13.4
3	41 -50	28	25.0
4	51 -60	29	25.9
5	>60	26	23.4
	TOTAL	112	100

Table 5.6 DM TYPES

	FREQUENCY	PERCENTAGE
TYPE I	3	2.7
TYPE II	109	97.3
TOTL	112	100

Table 5.7 DISTRIBUTIONS OF BS VALUES AND AGE

	BSL FASTING	BSL PP	AGE
Minimum	128	167	19
Maximum	388	506	71
Mean	182.91	286.33	49.7
Median	176	269	49.5
Standard deviation	47.187	66.134	13.19

Table 5.8 DM COMPLICATIONS

S. NO	COMPLICATION	FREQUENCY	PERCENTAGE
1	CAD	20	17.9
2	MET.SYN	20	17.9
3	DIA.RETINO	24	21.4
4	DIA.NEPHRO	15	13.4
5	PVD	15	13.4
6	D.NEURO	27	24.1

5.9 RISK FACTORS FOR DM COMPLICATIONS

Table 5.9.1 FBS >176 AND COMPLICATIONS

	PRESENT	ABSENT	ODD RATIO	CHI-SQUARE	P-VALUE
CAD	17	40	7.367	11.333	**0.001**
MET.SYN	15	42	3.571	5.666	**0.015**
D.RETINOPATHY	22	35	16.657	20.139	**0.0001**
D.NEPHROPATHY	13	44	7.83	8.869	**0.003**
PVD	11	46	3.049	3.89	**0.045**
D.NEUROPATHY	19	38	2.938	5.4	**0.017**

FBS>176 is significantly associated with all the complications

Table 5.9.2 PP>269 AND COMPLICATIONS

	PRESENT	ABSENT	ODD RATIO	CHI-SQUARE	P-VALUE
CAD	18	39	12.231	14.899	**0.0001**
MET.SYN	18	39	12.231	14.899	**0.0001**
D.RETINOPATHY	22	35	16.657	20.319	**0.0001**
D.NEPHROPATHY	14	43	17.581	12.482	**0.0001**
PVD	12	45	4.662	5.871	**0.014**
D.NEUROPATHY	22	35	6.286	13.319	**0.0001**

PP > 269 is significantly associated with all the skin lesions

Table 5.10 PATTERN OF SKIN LESIONS

SR.NO	SKIN DISEASES	FREQUENCY	PERCENTAGE
1	PRURITUS	14	12.5
2	DIABETIC DERMOPATHY	3	2.7
3	NECROBIOSIS DIABETICA LIPOIDICORAM	2	1.8
4	GRANULOMA ANNULARE	1	0.9
5	DIABETIC BULLAE	3	2.7
6	SCELERODERMA LIKE SYNDROME	4	3.6
7	DIABETIC FOOT	14	12.5
8	FUNGAL INFECTION	19	17
9	BACTERIAL INFECTION	14	12.5
10	XANTHOMA	2	1.8
11	INSULIN LIPODYSTROPHY	3	2.7
12	CHANGES IN NAIL	6	5.4
13	PERFORATING DERMATOSIS	7	6.3
14	VITILIGO	3	2.7
15	LICHEN PLANUS	4	3.6
16	BULLOUS PEMPHIGOIDS	1	0.9
17	DERMATITIS HERFATIFORMIS	2	1.8
18	PSOARISIS	3	2.7
19	ECZEMA	7	6.3
	TOTAL	112	100

The common presentations of the skin lesions are fungal infections followed by bacterial infection, diabetic foot, pruritis and perforating dermatosis.

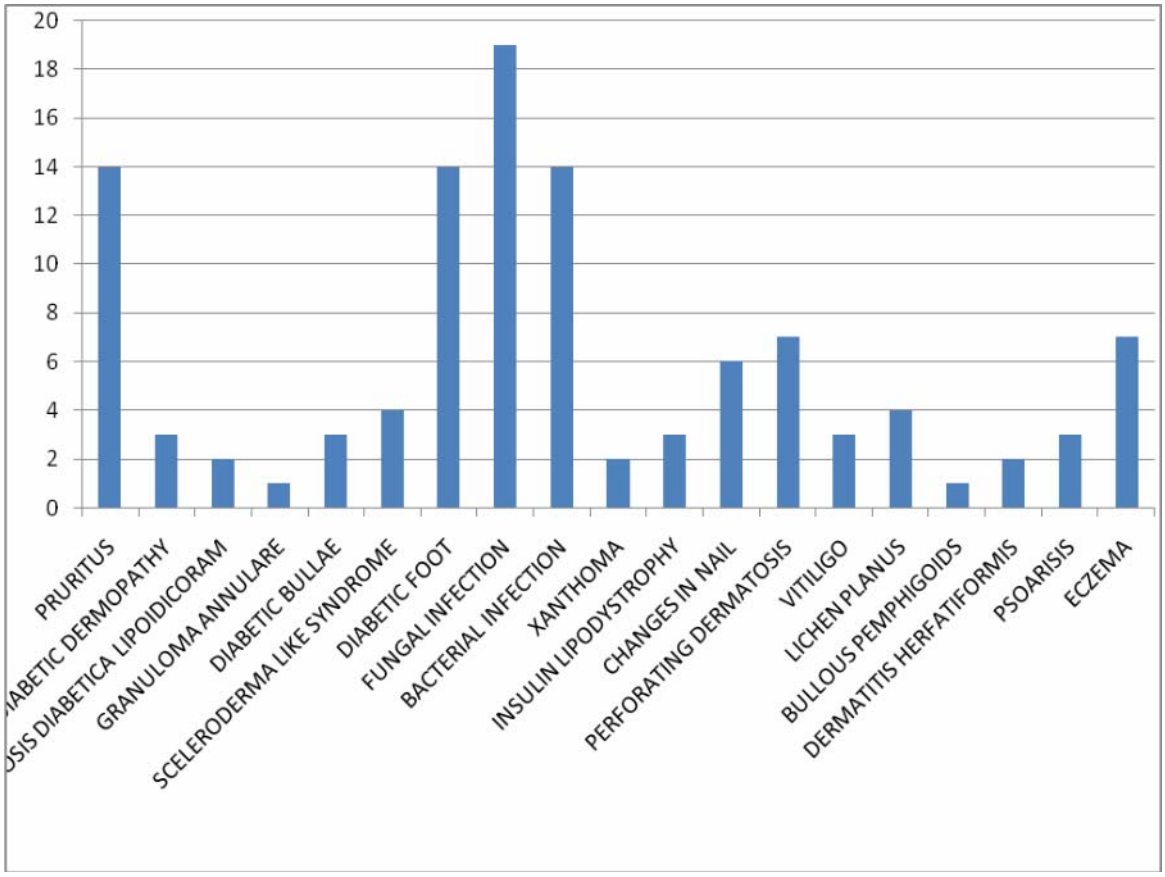

Fig. 5.10 Frequency pattern of skin lesions in diabetics.

5.11 RISK FACTORS ANALYSIS FOR SKIN LESIONS IN DM

Table 5.11.1. AGE>50 AND SKIN LESIONS

	PRESENT	ABSENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	3	52	0.241	4.905	**0.025**
DIABETIC FOOT	10	45	2.944	3.89	**0.046**
BACT.INFECTION	5	50	0.533	1.148	0.217
FUNGAL INFECTION	7	48	0.547	1.377	0.179
DERMATOSIS	3	50	0.764	0.117	0.521

Age more than 50 years is significantly associated with pruritis and diabetic foot.

Table 5.11.2 SEX AND SKIN LESIONS

SKIN LESION	SEX	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	MALE	8	49	1.333	0.25	0.416
	FEMALE	6	49			
DIABETIC FOOT	MALE	6	51	0.691	0.413	0.361
	FEMALE	8	47			
BACT.INFECTION	MALE	7	50	0.96	0.005	0.584
	FEMALE	7	48			
FUNGAL INFECTION	MALE	10	47	1.087	0.028	0.534
	FEMALE	9	46			
PERFORATING DERMATOSIS	MALE	3	54	0.708	0.193	0.48
	FEMALE	4	51			

Sex category is not having significant association with skin lesions.

Table 5.11.3. DM TYPE AND SKIN LESIONS

SKIN LESION	TYPE OF DM	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	TYPE I	0	3	1.147	0.44	0.667
	TYPE II	14	95			
DIABETIC FOOT	TYPE II	0	3		0.44	0.667
	TYPE II	14	95			
BACT.INFECTION	TYPE I	1	2	3.692	1.223	0.373
	TYPE II	13	96			
FUNGAL INFECTION	TYPE I	1	2	2.528	0.586	0.431
	TYPE II	18	91			
PERF.DERMATOSIS	TYPE I	1	2	8.583	3.859	0.178
	TYPE II	6	103			

DM type is not having the association with skin lesions.

Table 5.11.4 FBS > 176 AND SKIN LESIONS

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	5	52	0.49	1.475	0.171
DIABETIC FOOT	14	43	0.754	15.439	**0.001**
BACT.INFECTION	4	53	0.34	3.19	0.066
FUNGAL INFECTION	7	50	0.502	1.808	0.137
DERMATOSIS	4	53	1.308	0.117	0.52

FBS >176 is significantly associated with Diabetic foot.

Table 5.11.5 PP >269 AND SKIN LESIONS

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	5	52	0.491	1.478	0.177
DIABETIC FOOT	13	44	15.955	11.274	**0.001**
BACT.INFECTION	8	49	1.333	0.25	0.416
FUNGAL INFECTION	5	52	0.282	5.53	0.97
DERMATOSIS	4	53	1.308	0.117	0.52

PP >269 is significantly associated with Diabetic foot.

5.12. ASSOCIATION OF SKIN LESIONS WITH OTHER COMPLICATIONS OF DM

Table 5.12.1 CAD AND SKIN LESION

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	1	19	0.32	1.252	0.232
DIABETIC FOOT	3	17	1.299	0.139	0.475
BACT.INFECTION	2	18	0.741	0.139	0.525
FUNGAL INFECTION	0	20	1.26	4.979	**0.016**
DERMATOSIS	3	17	3.82	3.181	0.107

CAD is significantly associated with fungal infections

Table 5.12.2 METABOLIC SYNDROME AND SKIN LESIONS

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	1	19	0.32	1.252	0.235
DIABETIC FOOT	4	16	2.05	1.252	0.22
BACT.INFECTION	2	18	0.741	0.139	0.525
FUNGAL INFECTION	0	20	1.26	4.094	**0.016**
DERMATOSIS	2	18	1.933	0.584	0.365

Metabolic syndrome is significantly associated with fungal infection.

Table 5.12.3 DIABETIC RETINOPATHY AND SKIN

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	2	22	0.576	0.485	0.383
DIABETIC FOOT	7	17	4.765	7.75	**0.011**
BACT.INFECTION	2	22	0.576	0.485	0.383
FUNGAL INFECTION	0	24	1.275	5.24	**0.006**
DERMATOSIS	1	23	0.594	0.226	0.534

Diabetic Retinopathy is significantly associated with Diabetic foot and Fungal infection.

Table 5.12.4 DIABETIC NEPHROPATHY AND SKIN LESIONS

	PRE	AB	ODD	CHI-	P-

	SENT	SENT	RATIO	SQUARE	VALUE
PRURITIS	1	4	0.462	0.539	0.407
DIABETIC FOOT	2	13	1.09	0.011	0.593
BACT.INFECTION	1	24	0.462	0.539	0.407
FUNGAL INFECTION	0	15	1.244	3.638	**0.04**
DERMATOSIS	1	14	1.083	0.005	0.645

Diabetic Nephropathy is significantly associated with fungal infection

Table 5.12.5 PVD AND SKIN LESIONS

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	0	15	1.16	2.474	0.116
DIABETIC FOOT	3	12	1.955	0.891	0.281
BACT.INFECTION	0	15	1.69	2.474	0.116
FUNGAL INFECTION	0	18	1.244	3.538	**0.048**
DERMATOSIS	1	14	1.083	0.005	0.645

PVD is significantly associated with fungal infection

Table 5.12.6 DIABETIC NEUROPATHY AND SKIN LESIONS

	PRE SENT	AB SENT	ODD RATIO	CHI-SQUARE	P-VALUE
PRURITIS	0	27	1.192	5.082	**0.016**
DIABETIC FOOT	5	22	1.919	1.178	0.221
BACT.INFECTION	3	24	0.841	0.063	0.551
FUNGAL INFECTION	4	23	0.812	0.117	0.495
DERMATOSIS	3	24	2.531	1.435	0.22

Diabetic Neuropathy is significantly associated with pruritis.

6. DISCUSSION

During the study period of 2008 the total of 2462 cases were seen in the OPD till reaching the no 300 diabetes mellitus patients. So the prevalence of diabetic in general OPD is 12.2%.among these 2462 cases 222 patients had skin lesions. The prevalence is 9.1%. Of the 300 diabetic patients 61 had skin lesions. So the prevalence of skin lesions in diabetics is 20.3%. This is much higher than the prevalence of skin lesions in general population. It is supported by International Journal of diabetes in developing countries 2006[6]. Of the 300 diabetic patients 156 were male(52%) and 144 were female(48%). Type I diabetes mellitus was 18(6%) and the type II diabetes mellitus were 239(79.71%) and 43 were unclassified (14.3%). (Refer Table 5.1.1)

During the study period of 2009 the total of 2441 cases were seen in the OPD till reaching the no 300 diabetes mellitus patients. So the prevalence of diabetic in general OPD is 12.3%. Among these 2441 cases 186 patients had skin lesions. The prevalence is 7.61%. Of the 300 diabetic patients 51 had skin lesions. So the prevalence of skin lesions in diabetes mellitus is 17%. This is much higher than the prevalence of skin lesions in general population. Of the 300 diabetic patients 149 were male(49.6%) and 151 were female(51.4%). Type I diabetes mellitus was 16(5.3%) and the type II diabetes mellitus were 244(81.3%) and 40 were unclassified (13.3%). (Refer Table 5.1.2)

During the study period of 2008 and 2009 together the record of 729 Diabetic patients were reviewed. Of them376 were male (51.6%) 353 were female (48.4) . Of them 134 had skin lesion (18.4%). 69 were male (51.5%) and 120 were female(48.5..%).(Refer Table 5.2.1)

In the combined analysis the details of 1329 diabetic patients were taken for analysis. Of them 600 from OPD and 729 from IP. Of them 246(18.5) were having skin lesions. Of them 126 were male(51.2%) 120 were female(48.8%). So the female are almost equally affected by skin lesion in diabetics. (Refer Table 5.3)

In the OPD in 2008 and 2009 together totally 600 diabetics were seen. Of them 112 had skin lesion (61 in 2008 and 51 in 2009). These 112 patients were studied in details and taken for analysis. Of these 112 patients 55 were male(49.1%) and 57 were female(50.9%). There was no association of sex difference for skin lesions in diabetics(p value >0.05). (Refer Table 5.4)
Regarding the age distribution of 112 patients the range was from 19 to 71. they were divided into each decade there was progressively increasing trends of skin lesion in diabetics. (Refer Table 5.5)

The mean age of this study population were 49.70.so the age >50 and <50 were taken as cut off value for the analysis whether the age having significant risk on skin lesions in diabetics. There was significant association age >50 with occurrence of the skin lesions especially for pruritis and diabetic foot(p value <0.05) (Refer Table 5.7)

Of the 112 patients 3(2.7%) were had type I diabetes mellitus and109(97.3) were typeII diabetes mellitus. Here the typeI is far lesser than the usual prevalence. The reason is the type I is more common in childhood and they have been excluded in this study. (Refer Table 5.6)

The fasting and post prandial blood sugar value of these 112 patients were taken for analysis. The fasting BSL ranged from 128 to 388 mg%.the median value was 176. the post prandial BSL ranged from 167 to 506.The median value is was tken as cut off value for analyzing the correlation of the BSL with skin lesions in diabetics. (Refer Table 5.7)

Of the 112 diabetics with skin lesions the associated complications were analyzed. 20 (17.9%) had having CAD.20 (17.9%) had metabolic syndrome.24 (21.4%) of them had diabetic retinopathy. 15 (13.4) had having diabetic nephropathy. 15 (13.4) had diabetic peripheral vascular diseases. And 27(24.1%) of them had having diabetic neuropathy. (Refer Table 5.8)

The BSL as a risk factor for individual diabetic complications were analyzed. Fasting BSL >176 has statistically significant correlation with all the types of complications like CAD(P value 0.001), Metabolic syndrome(P value 0.015), Diabetic retinopathy(P value 0.0001), Diabetic nephropathy(P value 0.003), Peripheral vascular diseases(P value 0.045), and Diabetic neuropathy(P value 0.017), in the same way the post prandial BSL >269 also had the significant association with all the above said complications.

Post prandial value was more statistically significant correlation than the Fasting BSL value. (Refer Table 5.9.1. & 5.9.2)

On observing the pattern of skin lesions in DM patients, the occurrence of Fungal infections are the most common (17%) followed by Bacterial infection (12.5%), Diabetic foot (12.5%), Pruritis (12.5%) and Perforating Dermatosis (6.3%) are the other common skin lesions in Diabetics. (Refer Table 5.10)

The common presentations of the skin lesions observed in the study were further considered for the analysis of the association of the risk factors for the skin lesions in diabetics. Age > 50 was significantly associated with pruritis (P value 0.025) and diabetic foot P value 0.46). (Refer Table 5.11.1)

The Association of the sex with patters of the skin lesions were analyzed. Sex is not having the significant association with any if the common skin lesions. (Refer Table 5.11.2)

The type of diabetes is not having the significant association with any of the common skin lesions in diabetics in this study (P value>0.05). The reason for this observation in this study was due to selection of the cases. There was only 3 cases of type I diabetes mellitus patients with skin lesions because children were excluded where the Type I diabetes more common. (Refer Table 5.11.3)

Fasting BSL>176 is significantly associated with Diabetic foot (P value 0.001). (Refer Table 5.11.4) In the same way post prandial >269 is also significantly associated with diabetic Foot (P value 0.001) (Refer Table 5.11.5)

The Association of Diabetic complications in cases of skin lesions with diabetics were analyzed. CAD is significantly associated with fungal infection (P value 0.016). (Refer Table 5.12.1) Metabolic syndrome also significantly associated with fungal infection (P value 0.016) (Refer Table 5.12.2). Diabetic retinopathy is significantly associated with Diabetic Foot(P value0.011) and fungal infection (P value 0.006). (Refer Table 5.12.3) Diabetic nephropathy is significantly associated with fungal infection (P value 0.04). (Refer Table 5.11.4). Peripheral vascular diseases is also significantly associated with fungal infection (P value 0.48). (Refer Table 5.11.5) Diabetic neuropathy is significantly associated with pruritis (P value 0.016). (Refer Table 5.11.6)

From the above observation it is evident that fungal infections are significantly associated with CAD, Metabolic syndrome, Diabetic retinopathy, PVD (P value <0.05).

7. CONCLUSION

1. The prevalence of the skin lesion in General population is12.2%. The skin lesions in diabetes mellitus is 20.3%. The skin lesions in general population is 9.1%.
2. Increasing the Fasting and post prandial BSL has significant correlated with all the types of complications like CAD, Metabolic syndrome, Diabetic retinopathy, Diabetic nephropathy, Peripheral vascular diseases, and Diabetic neuropathy. Post prandial value was more statistically significant correlation than the Fasting BSL value.
3. Diabetes mellitus with fungal infections are significantly associated with diabetes complications like CAD, Metabolic syndrome, Diabetic retinopathy, Diabetic nephropathy and peripheral vascular diseases.
4. Diabetes mellitus with Diabetic Foot is significantly associated with Diabetic Retinopathy.
5. Diabetes mellitus with prurites is significantly associated with Diabetic Neuropathy.
6. The age >50 with occurrence of the skin lesions especially for pruritis and diabetic foot are common.

BIBLIOGRAPHY

1. Jennifer L, John E. Diabetes mellitus. *In*: Irvin MF, Arthur Z, Klaus W, Austen KF, Goldsmith LA, Katz SI, editors. Dermatology in General Medicine, 6 th ed. Mc Graw Hill. Medical Publishing Division: New York; 2003. p. 1651-61
2. Mahajan S, Koranne RV, Sharma SK. Cutaneous manifestations of diabetes mellitus. Indian J Dermatol Venerol Leprol 2003;69:105-8
3. Greenwood AM. A study of skin in 500 diabetics. JAMA 1927;89:774-9.
4. Yosipovitch G, Hodak E, Vardi P, Shraga I, Karp M, Sprecher E, *et al.* The prevalence of cutaneous manifestations in IDDM patients and their association with diabetes risk factors and microvascular complications. Diabetes Care 1998;21:506.
5. Harrison 'S Priciple Of Internal Medicine 17 ' Edi Vol Ii:2275-2304
6. Nigam Pk Panel S Et Al. Patterns Of Dermatosis In Diabetes 2003;69:2:83-85
7. 7.Yasmeen Et Al. Cutaneous Manifestation Of Diabetes.International Journal Of Diabetes In Developing Countries 2006;Vol 26:132-155 8.Chilukuri Sreedevi Et Al, Dematological Lesions In Diabetes Mellitus,Diabetalgia Croatica 31-3,2002
8. Romano G. et al. skin lesions in Diabetes mellitus: prevalence and clinical correlations. Diabetes res clin pract 1998;39:101-106

9. Yefmior AS,et al. pruritis in diabetes mellitus; Investigations of prevalence and correlation control. Diabetes care 1986;9;273-275
10. Binkley GW Dermatopathy in the diabetic syndrome. Arch Dermatol 1965;92;625-634
11. Rosenbloom AL. skeletal and joint manifestations of childhood Diabetes mellitus. Eur J pediatr 1990;149;380-388
12. Cruz PD hud JA. ezcess insulin binding to insulin like growth factor receptors; proposed mechanism for acanthosis nigricans. J invest Dermatol 1992;92 98.
13. Huntley ac cutaneous manifestation of diabetes mellitus arch Dermatol 1979;115;324-325
14. Sobel JD vulvovaginal candidiasis- What we do wnd do not know .Ann intern med 1984;101:391-392.
15. Petroz JW,Warthan Tl Malignant External Otitis.Arch Dermatol1974;110:258-260.
16. Hroon TS .Diabetes And Skin A Review. Scott Med 1974;19:257-267
17. Grunfeld C. Diabetic Foot Ulcers: Etiology Treatment And Prevention. Adv. Intern Med 1991;37:103-132.
18. Bleich Hl, Boro Es Diabetic Polyneuropathy;The Importance Of Insulin Deficiency,Hyperglycemia And Alteration In Myoinositol Metabolism In Its Pathogenesis. N Engl J Med 1976;295:1416-1420

19. Huntley ac. The cutaneous manifestations of diabetes mellitus. J Ann acad dermatol1982;7:427-455.
20. Blunn I, Schwab H. Le Treatment To Diabetes Sucrepar I' Insulin. Vouv Presse Med 1923;31:637-641.
21. Lon Cc Laidler P, Holt PJ A Suprabasal Acantholysis-An Unusual Feature Of Necrolytic Migratory Erethema. Cli Exp Dermatol 1993;18:464-467.
22. Brambilla L.Boneschi V De Blassio A Et Al. Sarcoma De Mediterraneo. Pathological Associate In Una Casuistica Di 100 Pazienti. G Ital Dermatol Venerol 1988;123:477-480
23. Freidman-Brinbaum R, Weltfield S Katzn I Kaposi Sarcoma; Retrospective Study Of 67 Cases With The Classical Form.Dermatologia1990;180:13-17.
24. Vion B, Frenk E Erworbene Reactive Kollgenase Des Erwachsenen: Erfolgriche Behandlung Durch UV-B Licht. Hautarzt1989;40:448-450
25. Lundstrom IM. Incidence Of Diabetes Mellitus In Patients With Oral Lichen Planus. Int J Oral Sur.1983;12:147-152.
26. Cruz PO, East C, Berstresser Pr. Dermal Subcutaneous And Tendon Xanthoma: Diagnostic Markers For Specific Lipo[Protein Disorders. J Am Acad Dermatol1988;19:95-111.
27. Parker F, Bagdade, JP Odland Gf Et Al. Evidence For The Chylomicron Origin Of The Lipid Accumulating In The Diabetic Eruptive Xantoma;

A Corletiva Lipid Biochemical Histochemical And Electron Microscope Study. J Clin Invest 1970;49:2172-2187

28. Perez Mi Kohn SR Et Al. Cutaneous Manifestations Of Diabetes Mellitus. J An Acad Dermatol 1994;30:519-531

PROFORMA

Patient Name :

Age :

Sex :

Ip/Op No :

Address :

Complaints :

History Of Present Illness:

Mode Of Onset

Activity At The Time Of Illness

Time Of Onset

Associated Symptoms

Haedache, Vomiting, Altered Sensorium

Past History :

Family History :

General Examination :

Wt :

BMI :

Pulse :

B P :

Peripheral Vascular Disease :

Funducopy :

CVS :

- S1 S2
- Murmur

RS :

- Air Entry
- Breath Sound

Abdomen :

- Organomegaly
- Free Fluid

CNS :

- Neuropathy

Skin Lesion :

- Pruritus
- Diabetic Dermopathy
- Necrobiosis Diabetica Lipoidicoram
- Granuloma Annulare
- Diabetic Bullae
- Sceleroderma Like Syndrome
- Diabetic Foot
- Fungal Infection
- Bacterial Infection

- Xanthoma
- Insulin Lipodystrophy
- Changes In Nail
- Perforating Dermatosis
- Vitiligo
- Lichen Planus
- Bullous Pemphigoids
- Dermatitis Herfatiformis
- Psoarisis
- Eczema

Complications of diabetes :

- CAD
- Metabolic syndrome
- Diabetic retinopathy
- Diabetic nephropathy
- Pvd
- Diabetic neuropathy

Investigation :

- Blood sugar level -Ffasting/ Post prandial
- Blood urea
- Serum creatinine
- Lipid profile

Fig-1 **Fig-2**

Necrobiosis Lipoidica Diabeticorum (NLD)

Fig-3 **Fig-4**

Diabetic Neuropathy of Foot **Granuloma Annulare**

Fig-5

Diabetic Thick Skin

Fig-6

Spantaneous Blisters in Diabetes

Fig-7
Fungal Infection(Tinea cruris) with DM

Fig-8
Candidal infection with DM

Fig-9

Bacterial Infection With DM

Fig-10

Eruptive xanthoma with DM

Fig-11

Fig-12

Diabetic Dermopathy

Fig-13

Periungual Telangiectasia

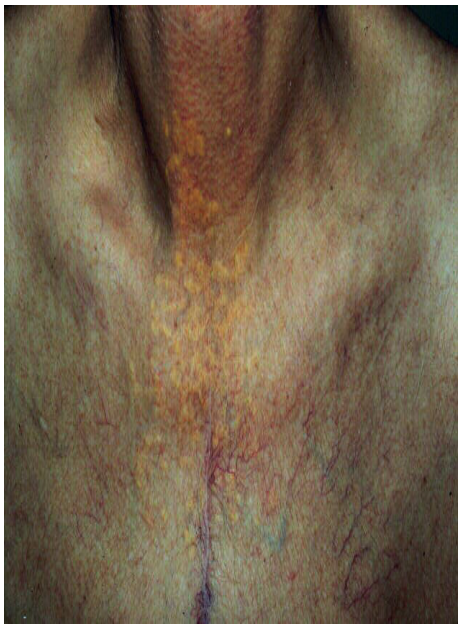

Fig-14

Xanthelasma

Fig-15

Pigmented purpura

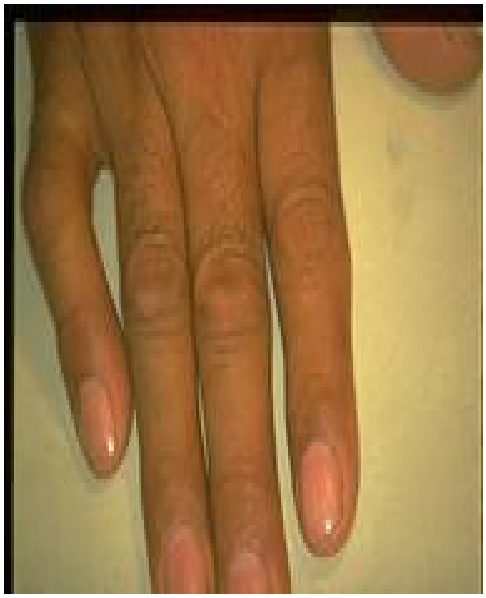

Fig-16

Diabetic hand syndrome

MASTER CHART

SR. NO	AGE	SEX	DM TYPE	BSL F	BSL PP	Type of Skin Lesions (Table 5.10)	CAD	MET.SYN	D.RETINO	D.NEPHR	PVD	D.NEURO
1	30	M	2	138	224	8						
2	44	M	2	144	356	10		YES				
3	44	F	2	165	306	14		YES		YES		
4	46	M	2	134	210	19						YES
5	48	F	2	130	240	1						
6	58	M	2	237	350	7	YES	YES	YES	YES		
7	62	F	2	150	198	1						
8	24	F	1	178	320	9						YES
9	58	M	2	142	213	8						YES
10	60	M	2	130	310	1						
11	48	M	2	142	234	9						
12	52	F	2	140	201	8						
13	55	F	2	282	356	7						YES
14	44	M	2	165	406	2		YES	YES	YES	YES	YES
15	48	F	2	152	388	13						
16	52	F	2	162	231	19						
17	62	M	2	172	253	13	YES					
18	67	F	2	183	319	2	YES	YES		YES		
19	19	M	1	198	412	8						YES
20	48	M	2	146	230	1						
21	44	M	2	210	310	7	YES	YES	YES			
22	39	F	2	142	219	8						

SR. NO	AGE	SEX	DM TYPE	BSL F	BSL PP	Type of Skin Lesions (Table 5.10)	CAD	MET.SYN	D.RETINO	D.NEPHR	PVD	D.NEURO
23	48	M	2	132	298	19					YES	
24	52	F	2	139	294	8						
25	28	M	2	187	328	1						
26	39	F	2	158	296	10		YES				YES
27	42	M	2	176	289	17						YES
28	48	F	1	200	329	13						
29	59	M	2	276	348	7			YES			
30	57	F	2	158	242	9						
31	34	M	2	187	410	1		YES	YES	YES		
32	68	M	2	208	265	18						
33	49	F	2	136	256	1						
34	38	M	2	145	240	15						
35	62	F	2	208	355	6	YES		YES	YES		YES
36	61	M	2	145	209	8						
37	58	M	2	193	388	9	YES	YES	YES	YES		YES
38	44	F	2	153	210	12						
39	29	F	2	142	272	9						
40	52	F	2	128	230	5						
41	49	M	2	210	344	7		YES	YES		YES	YES
42	66	F	2	134	243	13						YES
43	67	F	2	178	417	12	YES		YES	YES	YES	
44	39	M	2	234	231	8						
45	49	F	2	278	210	7						
46	58	F	2	143	230	9						

SR. NO	AGE	SEX	DM TYPE	BSL F	BSL PP	Type of Skin Lesions (Table 5.10)	CAD	MET.SYN	D.RETINO	D.NEPHR	PVD	D.NEURO
47	54	M	2	150	280	14						
48	70	M	2	156	356	2	YES	YES	YES		YES	YES
49	68	F	2	144	298	3	YES					
50	63	M	2	132	217	9						
51	59	F	2	188	267	6	YES	YES			YES	
52	48	F	2	177	301	1						
53	55	M	2	198	312	4					YES	YES
54	28	F	2	143	219	1						
55	59	F	2	188	254	8						
56	49	M	2	256	329	13	YES	YES		YES		YES
57	63	F	2	245	398	7						
58	69	M	2	214	321	5						
59	70	F	2	211	243	18				YES		
60	67	F	2	132	243	12						
61	51	M	2	202	256	6						
62	38	F	2	187	234	13		YES	YES		YES	YES
63	55	F	2	198	298	11		YES	YES		YES	YES
64	27	M	2	143	254	19						
65	39	M	2	178	276	8						YES
66	32	F	2	145	245	15						
67	59	M	2	199	312	7						
68	42	M	2	145	243	9						
69	61	M	2	205	278	7	YES		YES			
70	32	F	2	176	213	19						

SR. NO	AGE	SEX	DM TYPE	BSL F	BSL PP	Type of Skin Lesions (Table 5.10)	CAD	MET.SYN	D.RETINO	D.NEPHR	PVD	D.NEURO
71	45	M	2	167	254	15						YES
72	49	F	2	134	213	8						
73	71	F	2	156	239	8						
74	29	M	2	172	219	19						
75	62	F	2	256	321	7					YES	YES
76	39	M	2	167	243	8						
77	48	M	2	199	265	17						
78	37	F	2	165	388	8						YES
79	29	F	2	165	269	9						
80	62	M	2	269	389	7		YES				
81	57	F	2	178	249	14			YES			
82	49	M	2	160	254	16					YES	
83	31	F	2	143	210	8						
84	25	M	2	132	211	1						
85	59	M	2	298	438	12	YES	YES	YES	YES		YES
86	62	F	2	204	349	11	YES		YES	YES		
87	37	M	2	145	239	9						
88	60	M	2	138	232	19						
89	23	M	2	152	219	8						
90	52	F	2	388	506	11		YES	YES		YES	
91	50	M	2	198	230	15						
92	49	M	2	138	204	1						
93	46	F	2	306	408	7						
94	55	F	2	188	269	12						

SR. NO	AGE	SEX	DM TYPE	BSL F	BSL PP	Type of Skin Lesions (Table 5.10)	CAD	MET.SYN	D.RETINO	D.NEPHR	PVD	D.NEURO
95	66	M	2	209	299	3	YES		YES	YES		
96	71	F	2	231	378	6	YES	YES		YES	YES	
97	22	F	2	154	218	1						
98	52	F	2	188	298	8						
99	29	M	2	198	278	9						
100	43	F	2	166	298	9						
101	49	M	2	188	245	8						
102	37	M	2	187	254	1						
103	68	F	2	254	276	5	YES		YES		YES	YES
104	70	M	2	179	354	1	YES		YES			
105	69	M	2	145	167	18						
106	28	F	2	187	261	8						
107	58	M	2	276	312	13	YES					
108	67	F	2	232	324	7						YES
109	52	M	2	178	265	12						
110	39	F	2	145	324	9						
111	55	M	2	276	444	7			YES	YES	YES	
112	59	M	2	273	389	9	YES	YES	YES			YES